

THE SYNTHESIS OF TETRAHYDRONAPHTHOIC ACIDS

BY

WILLIAM KAPLAN

B.A., New York University, 1940

M.A., University of Illinois, 1941

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE SCHOOL OF THE
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THE SYNTHESIS OF TETRAHYDRONAPHTHOIC ACIDS

A method of synthesis of 6-methoxy-1,2,3,4-tetrahydro-1-naphthoic acid was desired as a starting point in the synthesis of naphthalene analogs of sterol hormones.

The first route to the substituted tetrahydronaphthoic acids which was studied was the reaction between ethyl tetrahydrofuroate and benzene derivatives. It had been shown¹ that furoic acid and benzene derivatives reacted in the presence of aluminum chloride to give 6-substituted-1-naphthoic acids. It was hoped that if furoic acid were replaced by tetrahydrofuroic acid the corresponding tetrahydronaphthoic acid might be obtained instead of the naphthoic acid. Unfortunately experiment did not justify these hopes.

The reaction of γ -anisyl- γ -butyrolactone with potassium cyanide was studied in an attempt to prepare γ -anisyl- γ -cyano-butyric acid. If the latter compound were subjected to ring closure, reduction of the resulting ketone, and hydrolysis of the cyano group the desired 6-methoxy-1,2,3,4-tetrahydro-1-naphthoic acid would be obtained. However, the product finally obtained was shown to be 6-methoxy-1,2,3,4-tetrahydro-2-naphthoic acid, indicating that the reaction of potassium cyanide with γ -anisyl- γ -butyrolactone involves a rearrangement leading to the formation of γ -anisyl- β -cyanobutyric acid.

A similar rearrangement was observed by Blaise³ who found that the reaction of potassium cyanide with γ -methyl- γ -valerolactone yielded γ -methyl- β -cyanovaleric acid instead of the expected γ -cyano acid.

The structure of 6-methoxy-1,2,3,4-tetrahydro-2-naphthoic acid was established by dehydrogenation with sulfur or palladium on charcoal to yield 6-methoxy-2-naphthoic acid. The identity of the dehydrogenation product was established by its melting point, the melting point of its amide and by a mixed melting point of each with authentic samples. The authentic 6-methoxy-2-naphthoic acid was prepared according to the directions of Fries and Schimmlschmidt⁴ by the following series of conversions: β -naphthol; 1,6-dibromo-2-naphthol; 1-6-dibromo-2-methoxynaphthalene; 6-bromo-2-methoxynaphthalene; 6-methoxy-2-naphthoic acid.

A third route to the tetrahydronaphthoic acids was the reduction with sodium and alcohol of the naphthoic acids. Reduction of 6-methoxy-1-naphthoic acid and 6-hydroxy-1-naphthoic acid gave interconvertible products which were shown to be the tetrahydro-derivatives by analysis. The behavior of the reduction products with bromine water indicated that the reduced ring was the one containing the carboxyl group.

EXPERIMENTAL

β -Anisoylpropionic acid.—Following the directions of Fieser and Hershberg⁵ a 95% yield of β -anisoylpropionic acid, m.p. 144°, was obtained from the reaction between anisole (302 g.) and succinic anhydride (294 g.) in the presence of aluminum chloride (777g.) when the precaution was taken of finely powdering the succinic anhydride crystals.

γ -Anisyl- γ -butyrolactone.—The keto-acid (140 g.) was added to 1 l. of absolute ethyl alcohol and the solution refluxed for several days, water being removed by calcium carbide in a Soxhlet extractor. Upon completion of esterification the excess alcohol was removed by distillation and 500 cc. of isopropyl alcohol and 85 g. of vacuum-distilled aluminum isopropylate were added. Distillate boiling at 60° was very slowly removed through a fractionating column until ten drops failed to give a precipitate with a dilute hydrochloric acid solution of 2,4-dinitrophenylhydrazine. The isopropyl alcohol was then removed by distillation and excess 20% sulfuric acid added. The organic layer and the ether washings of the aqueous layer were combined and extracted with sodium hydroxide solution. The material remaining in the ether was refluxed for several hours with sodium hydroxide solution after removal of the ether by distillation. This sodium hydroxide solution was then washed with ether and added to the previous sodium hydroxide solution. The combined solutions were acidified and kept on the steam cone for an hour. The organic layer was taken up in ether and washed with dilute sodium bicarbonate solution. The ether solution was concentrated and placed in the ice-box for several days. The lactone crystallized; filtration yielded 96 g. (79%) of γ -anisyl- γ -butyrolactone.

γ -Anisyl- β -cyanobutyric acid.—The lactone (101 g.) and dried potassium cyanide (100 g.) in small crystals were put in a flask which had been dried in a Bunsen flame. A mechanical stirrer was attached. Dry nitrogen was passed slowly into the flask, which was kept at 210° for three and a half hours. The cold mass was dissolved in water and washed with ether. The water solution was acidified under the hood, cooled and extracted with ether. The ether was extracted with sodium bicarbonate solution and the dissolved ether was removed from the bicarbonate solution at room temperature by bubbling air through the solution. When the bicarbonate solution was acidified a brown oil separated which solidified in a few hours. The solid mass was washed several times with cold benzene until the washings were colorless. A yield of 36 g. of tan solid was obtained which was used directly in the next step. Pure crystals for analysis and neutral equivalent were obtained by extraction of the light tan solid with a mixture of 50% benzene and 50% heptane in which the compound was moderately soluble at elevated temperatures. The pure *γ -anisyl- γ -cyanobutyric acid* melted at 116.5° (cor.).

The reaction mixture must be worked up in the cold or an oily tar will be obtained which can only be purified by chromatographic adsorption on alumina.

6-Methoxy-4-keto-1,2,3,4-tetrahydro-2-naphthamide — Usual methods of ring closure, such as treatment with sulfuric acid or treatment of the acid chloride with aluminum chloride were unsuccessful. A sample of light tan cyano-acid (35 g.) was poured into a stainless steel bomb (250-cc. capacity) almost full of anhydrous hydrogen fluoride. The bomb was sealed and heated at 100° for one hour. The hydrogen fluoride was then allowed to evaporate for two days. Ether was poured into the bomb and the contents of the bomb transferred to a beaker. Water and sodium bicarbonate were added till the solution was neutralized. The brownish precipitate was separated and extracted with boiling alcohol. The alcohol was evaporated and the resulting tar was extracted several time with boiling water. When no more material could be extracted from the tar, concentrated sulfuric acid was added to it. After a week the acid was diluted with water and the tar was boiled with 20% sodium hydroxide. The

small white residue thus obtained was added to the material previously extracted from the tar and the whole was washed with dilute sodium hydroxide and recrystallized from water. A yield of 10 g. of 6-methoxy-4-keto-1,2,3,4-tetrahydro-2-naphthamide, m.p. 178° (cor.), was obtained.

The oxime was prepared following the directions of Shriner and Fuson,⁶ m.p. 217-219° (cor.).

6-Methoxy-1,2,3,4-tetrahydro-2-naphthamide. — The amide (400 mg.) and 0.4 g. of 10 per cent palladium on charcoal were put in a citrate bottle and 40 cc. of absolute alcohol added. The bottle was put in a shaker under 41 lbs. pressure of hydrogen for two hours. The catalyst was then removed by filtration and the alcohol evaporated. The residue was washed with ether and recrystallized from boiling water. A yield of 250 mg. (68%) of 6-methoxy-1,2,3,4-tetrahydro-2-naphthamide, m.p. 141° (cor.), was obtained.

6-Methoxy-1,2,3,4-tetrahydro-2-naphthoic Acid.—A sample of 0.866 g. of the amide in 12 cc. of hydrochloric acid, 12 cc of water and 8 cc. of glacial acetic acid was refluxed for three hours. The precipitate was removed by filtration and dissolved in sodium bicarbonate solution. The solution was acidified after treatment with Norite. The original mother liquor was evaporated to a small volume and the precipitate worked up with the main fraction. A yield of 0.730 g (85%) of 6-methoxy-1,2,3,4-tetrahydro-2-naphthoic acid, m.p. 151° (cor.), was obtained.

Dehydrogenation to 6-Methoxy-2-naphthoic Acid.—The amide (0.389 g.) and sulfur (0.140 g.) were heated at 210-245° for twenty minutes. The reaction mixture was sublimed at 5 mm. and sulfur removed from the sublimate with concentrated sodium sulfide solution. The residue was digested with alcohol and recrystallized from benzene. The product melted at 225° and gave a positive test for sulfur upon elementary analysis. This substance was probably the thio-amide. The amide was hydrolyzed with an alcoholic potassium hydroxide solution and an acid was obtained which melted at 194-196°. Dehydrogenation of the 6-methoxy-1,2,3,4-tetrahydro-2-naphthoic acid with sulfur also gave a product melting at 194-196°. The same compound was also obtained by catalytic dehydrogenation of the acid with palladium on charcoal.

An authentic sample of 6-methoxy-2-naphthoic acid prepared by the method of Fries and Schimmlschmidt⁴ sintered at 186° and melted at 196°. It displayed the same characteristics when mixed with the dehydrogenation product. (Fries and Schimmlschmidt⁴ reported that the acid sintered at 190° and melted at 209°).

An authentic sample of 6-methoxy-2-naphthamide, prepared from the authentic acid by the method of Shriner and Fuson,⁶ melted at 220-221° (lit.,³ 219°). The amide prepared from the dehydrogenation product melted at the same point as also did a mixture of the authentic and dehydrogenation samples.

SUMMARY

The reaction between potassium cyanide and γ -anisyl- γ -butyrolactone resulted in the formation of γ -anisyl- β -cyanobutyric acid. The successful conversion of this cyano acid to 6-methoxy-4-keto-1,2,3,4-tetrahydro-2-naphthamide and 6-methoxy-1,2,3,4-tetrahydro-2-naphthoic acid has been described.

BIBLIOGRAPHY

1. McCorkle and Turck, *Proc. Iowa Acad. Sci.*, **43**, 205 (1936).
Price, Chapin, Goldman, Krebs and Shafer, *J. Am. Chem. Soc.*, **63**, 1857 (1941).
2. Wislicenus, *Ann.*, **233**, 101 (1886).
3. Blaise, *Compt. rend.*, **124**, 89 (1897).
4. Fries and Schimmlschmidt, *Ber.*, **58**, 2840 (1925).
5. Fieser and Hershberg, *J. Am. Chem. Soc.*, **58**, 2314 (1936).
6. Shriner and Fuson, "Identification of Organic Compounds," 2nd edition, John Wiley and Sons, New York, 1940.

VITA

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